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PENNIE & EDMONDS LLP
1667 K STREET NW
SUITE 1000
WASHINGTON, DC 20006

EXAMINER
NOGUEROLA, ALEXANDER STEPHAN

ART UNIT	PAPER NUMBER
1753	4

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/874,331	LIU ET AL.
	Examiner	Art Unit
	ALEX NOGUEROLA	1753

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) *1-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-27* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claim Rejections - 35 USC § 112

1. Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 20 requires that a sample volume be simultaneously separated in the absence of an electrical field and by electrophoresis; that is, in the presence of an electrical field. An electrical field cannot be simultaneously present and absent over the same region.

2. Claims 21-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 21 and 27 require that a sample components be simultaneously separated in the absence of an electrical field and by electrophoresis; that is, in the presence of an electrical field. An electrical field cannot be simultaneously present and absent over the same region.

3. Claims 3, 6-18, and 21-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:

a) Claims 3, 8, and 13: does the peak actually generate a fluorescence spectrum?

b) Claim 6, line 6: should "volumes" be -- channels --?

c) Claim 12, line 7: should "volumes" be -- channels --?

d) Claim 12: what is the relationship between a "sample component" and a volume (such as "a first volume" in line 7)?

e) Claim 12, line 5: -- after the first separation – should be inserted between "components" and ",";

f) Claim 17, line 1: -- substantially -- should be inserted between "the" and "isolated";

g) Claim 18 recites the limitation "the isolated volumes" in line 7. There is insufficient antecedent basis for this limitation in the claim;

h) Claims 21 and 27: the distinctions between "the sample components", "a plurality of sample components", and "a plurality of isolated sample volumes" are not clear; and

i) Claim 26 recites the limitation "each reference sample" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

4. Note that dependent claims will have the deficiencies of base and intervening claims.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-4, 12, 13, 17, and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yeung et al. (US 6,387,234 B1) in view of Chen (US 5,139,630).

Addressing claim 1, the Yeung et al. reference teaches a method for separating components of a sample (the abstract), comprising

obtaining a first separation of the sample components, wherein the first separation can be performed in the absence of an applied electric field (col. 6, ll. 26-38);

using an electric field to obtain a second separation of the sample components within a plurality of substantially isolated channels (col. 6, ln. 63 – col. 7, ln. 12); and

obtaining an intensity-time data record from each of the isolated channels, the intensity-time data records containing peaks (Figures 6 and 8).

The Yeung et al. reference does not specifically mention normalizing a migration time of a first peak with respect to a migration time of at least a second peak to correct for migration time differences between the isolated channels, although it should be noted that the Yeung et al. reference does disclose using software for normalizing the electropherograms (col. 22, ll. 14-16).

The Chen reference teaches normalizing a migration time of a first peak with respect to a migration time of at least a second peak to correct for migration time differences of the same compounds between different runs (col. 2, ln. 41 – col. 3, ln.22 and col. 3, ln. 24 – col. 4, ln. 24).

It would have been obvious to one with ordinary skill in the art at the time the invention was made to normalize a migration time of a first peak with respect to a migration time of at least a second peak as taught by the Chen reference in the invention taught by the Yeung et al. reference because this will allow rapid and reliable identification of sample peaks without resort to visual identification guesswork (col. 3, ll. 13-22 in the Chen reference).

Addressing claims 2 and 22, as seen in col. 10, ll. 60-65 of the Chen reference a reference sample is injected into electrophoresis capillary with other sample components.

Addressing claims 3 and 23, although the Yeung et al. reference as modified by the Chen reference does not mention whether the second peak has a different fluorescence spectrum

from other sample components, it would have been obvious to one with ordinary skill in the art at the time the invention was made to let the second peak have a different fluorescence so that it can be readily recognized. If the sample component corresponding to the second peak has the same or similar fluoresce spectrum as another sample component then it is likely the second peak will be larger than expected or substantially overlap another peak, thus making it more difficult to accurately determine the migration time of the second peak. Also, the Yeung et al. reference teaches a two-dimensional detector (col. 14, ll. 4-7).

Addressing claim 4, as seen in col. 4, ll. 3-24 of the Chen et al. reference normalizing a migration time comprises determining a ratio of the migration time of the first peak and the migration time of the second peak.

Addressing claim 12, the Yeung et al. reference teaches a system for separating components of a sample (the abstract), comprising

a first component for obtaining a first separation of the sample components, wherein the first separation can be performed in the absence of an applied electric field (col. 6, ll. 26-38);

a second component for electrophoretically separating each of the sample components, the second component comprising a plurality of substantially isolated channels (col. 6, ln. 63 – col. 7, ln. 12); and

The Yeung et al. reference does not specifically mention a processor to normalize a migration time of a first volume within one of the separation channels with respect to a migration

time of at least a second volume of the same separation channel to adjust for migration time difference between the isolated channels, although it should be noted that the Yeung et al. reference does disclose using software for normalizing the electropherograms (col. 22, ll. 14-16).

The Chen reference teaches a processor for normalizing a migration time of a first volume with respect to a migration time of at least a second volume to correct for migration time differences of the same compounds between different runs (col. 2, ln. 41 – col. 3, ln.22 and col. 3, ln. 24 – col. 4, ln. 24).

It would have been obvious to one with ordinary skill in the art at the time the invention was made provide a processor to normalize a migration time of a first volume with respect to a migration time of a second volume as taught by the Chen reference in the invention taught by the Yeung et al. reference because this will allow rapid and reliable identification of sample peaks without resort to visual identification guesswork (col. 3, ll. 13-22 in the Chen reference).

Addressing claim 13, although the Yeung et al. reference as modified by the Chen reference does not mention whether the presence of the second volume is indicated by a peak having a fluorescence spectrum different from other sample components, it would have been obvious to one with ordinary skill in the art at the time the invention was made to let the second volume have a different fluorescence spectrum so that it can be readily recognized. If the second volume has the same or similar fluoresce spectrum as another volume then it is likely the second volume spectrum will overlap the spectrum of another volume, thus making it more difficult to accurately determine the migration time of the other volume. Also, the Yeung et al. reference teaches a two-dimensional detector (col. 14, ll. 4-7).

Addressing claim 17, a substrate defining a plurality of channels therein is implied by col. 26, ll. 37-39 and element 33 in Figure 3 of the Yeung et al. reference, which teaches a holder on a translation stage for adjusting and tilting the isolated separation channels.

Addressing claim 20, the Yeung et al. reference teaches a method for separating components of a sample (the abstract), comprising

obtaining a first separation of the sample components into a first plurality of sample volumes in the absence of an applied electric field (col. 6, ll. 26-38);

after the first separation, simultaneously obtaining an electrophoretic separation of sample components present in each of the of the first plurality of sample volumes, wherein sample components present in different sample volumes are separated in a respective one of a plurality of substantially isolated separation channels (col. 6, ln. 63 – col. 7, ln. 12); and

obtaining an intensity-time data record from each of the isolated channels, the intensity-time data records containing peaks (Figures 6 and 8).

The Yeung et al. reference does not specifically mention normalizing a migration time of a first peak with respect to a migration time of at least a second peak to correct for migration time differences between the isolated channels, although it should be noted that the Yeung et al. reference does disclose using software for normalizing the electropherograms (col. 22, ll. 14-16).

The Chen reference teaches normalizing a migration time of a first peak with respect to a migration time of at least a second peak to correct for migration time differences of the same compounds between different runs (col. 2, ln. 41 – col. 3, ln.22 and col. 3, ln. 24 – col. 4, ln. 24).

It would have been obvious to one with ordinary skill in the art at the time the invention was made to normalize a migration time of a first peak with respect to a migration time of at least a second peak as taught by the Chen reference in the invention taught by the Yeung et al. reference because this will allow rapid and reliable identification of sample peaks without resort to visual identification guesswork (col. 3, ll. 13-22 in the Chen reference).

Addressing claim 21, the Yeung et al. reference teaches a method for separating components of a sample (the abstract), comprising

obtaining a first separation of the sample components into a first plurality of sample components in the absence of an applied electric field (col. 6, ll. 26-38); and

after the first separation, simultaneously obtaining an electrophoretic separation of each of the first plurality of sample components to thereby form a plurality of substantially isolated volumes from each of the plurality of sample components (col. 6, ln. 63 – col. 7, ln. 12).

The Yeung et al. reference does not specifically mention normalizing a migration time of at least one of the substantially isolated volumes with respect to a migration time of at least a second substantially isolated volume to correct for migration time difference between the isolated volumes, although it should be noted that the Yeung et al. reference does disclose using software for normalizing the electropherograms (col. 22, ll. 14-16).

The Chen reference teaches normalizing a migration time of a first peak from a first volume with respect to a migration time of at least a second peak from a second volume to correct for migration time differences of the same compounds between different runs (col. 2, ln. 41 – col. 3, ln.22 and col. 3, ln. 24 – col. 4, ln. 24).

It would have been obvious to one with ordinary skill in the art at the time the invention was made to normalize a migration time of a first peak with respect to a migration time of at least a second peak as taught by the Chen reference in the invention taught by the Yeung et al. reference because this will allow rapid and reliable identification of sample peaks without resort to visual identification guesswork (col. 3, ll. 13-22 in the Chen reference).

8. Claims 6-9, 11, 18, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yeung et al. (US 6,387,234 B1) in view of Liu et al. (US 5,228,690).

Addressing claim 6, the Yeung et al. reference teaches a method for separating components of a sample (the abstract), comprising

obtaining a first separation of the sample components, wherein the first separation can be performed in the absence of an applied electric field (col. 6, ll. 26-38);

using an electric field to obtain a second separation of the sample components within a plurality of substantially isolated channels (col. 6, ln. 63 – col. 7, ln. 12); and

obtaining an intensity-time data record from each of the isolated channels, the intensity-time data records containing peaks (Figures 6 and 8).

The Yeung et al. reference does not specifically mention normalizing an intensity of a first peak with respect to an intensity of at least a second peak to correct for intensity differences between the isolated channels, although it should be noted that the Yeung et al. reference does disclose using software for normalizing the electropherograms (col. 22, ll. 14-16).

The Liu et al. reference teaches a three-step normalization involving (1) baseline normalization; (2) absorbance normalization; and (3) time normalization (col. 8, ll. 34-36). Absorbance normalization involves normalizing an intensity of a first peak with respect to an intensity of at least a second peak to correct for intensity differences between different electrophoresis runs (col. 8, ln. 45 – col. 9, ln. 12).

It would have been obvious to one with ordinary skill in the art at the time the invention was made to normalize intensities as taught by the Liu et al. reference in the invention of the Yeung et al. reference because then the electropherograms can be accurately compared, with distortions due to a difference in sample volumes, for example (col. 9, ll. 43-49 in the Liu et al. reference).

Addressing claim 7, the Liu et al. reference teaches that second peak may be due to a marker compound (col. 9, ll. 7-10).

Addressing claim 8, although the Yeung et al. reference as modified by the Liu et al. reference does not mention whether the second peak has a different fluorescence spectrum from

other sample components, it would have been obvious to one with ordinary skill in the art at the time the invention was made to let the second peak have a different fluorescence so that it can be readily recognized. If the sample component corresponding to the second peak has the same or similar fluoresce spectrum as another sample component then it is likely the second peak will be larger than expected or substantially overlap another peak, thus making it more difficult to accurately determine the migration time of the second peak. Also, the Yeung et al. reference teaches a two-dimensional detector (col. 14, ll. 4-7).

Addressing claim 9, determining a ratio of the intensity first peak and the intensity of the second peak is implied by col. 8, ll. 48-51 and col. 8, ll. 59-64 of the Liu et al. reference, which teaches proportionally scaling the intensity of the first peak relative to the intensity of the second peak.

Addressing claim 11, that the peak intensity is a peak area is implied by col. 9, ll. 2-4 of the Liu et al. reference, which teaches that the relative peak areas remain the same after normalization.

Addressing claim 18, the Yeung et al. reference teaches a system for separating components of a sample (the abstract), comprising

a component for obtaining a first separation of the sample components, wherein the first separation can be performed in the absence of an applied electric field (col. 6, ll. 26-38);

an electrophoresis component for obtaining a second separation of the sample components within a plurality of substantially isolated channels (col. 6, ln. 63 – col. 7, ln. 12); and

a detector configured to obtain an intensity-time data record from each of the isolated channels, the intensity-time data records containing peaks (col. 14, ll. 4-15 and Figures 6 and 8).

The Yeung et al. reference does not specifically mention a processor configured to normalize an intensity of a first peak with respect to an intensity of at least a second peak to correct for intensity differences between the isolated channels, although it should be noted that the Yeung et al. reference does disclose using software for normalizing the electropherograms (col. 22, ll. 14-16).

The Liu et al. reference teaches a processor configured for performing a three-step normalization involving (1) baseline normalization; (2) absorbance normalization; and (3) time normalization (col. 12, ll. 67-68 and col. 8, ll. 34-36). Absorbance normalization involves normalizing an intensity of a first peak with respect to an intensity of at least a second peak to correct for intensity differences between different electrophoresis runs (col. 8, ln. 45 – col. 9, ln. 12).

It would have been obvious to one with ordinary skill in the art at the time the invention was made to configure a processor to normalize intensities as taught by the Liu et al. reference in the invention of the Yeung et al. reference because then the electropherograms can be accurately compared, with distortions due to a difference in sample volumes, for example (col. 9, ll. 43-49 in the Liu et al. reference).

Addressing claim 27, the Yeung et al. reference teaches a method for separating components of a sample (the abstract), comprising

obtaining a first separation of the sample components into a first plurality of sample components in the absence of an applied electric field (col. 6, ll. 26-38); and

after the first separation, simultaneously obtaining an electrophoretic separation of each of the first plurality of sample components to thereby form a plurality of substantially isolated volumes from each of the plurality of sample components (col. 6, ln. 63 – col. 7, ln. 12).

The Yeung et al. reference does not specifically mention normalizing an intensity of a first substantially isolated volume with respect to an intensity of at least a second substantially isolated volume to correct for intensity differences between the isolated volumes, although it should be noted that the Yeung et al. reference does disclose using software for normalizing the electropherograms (col. 22, ll. 14-16).

The Liu et al. reference teaches a three-step normalization involving (1) baseline normalization; (2) absorbance normalization; and (3) time normalization (col. 8, ll. 34-36). Absorbance normalization involves normalizing an intensity of a first peak of a frits volume with respect to an intensity of at least a second peak from a second volume to correct for intensity differences between different electrophoresis runs (col. 8, ln. 45 – col. 9, ln. 12).

It would have been obvious to one with ordinary skill in the art at the time the invention was made to normalize intensities as taught by the Liu et al. reference in the invention of the Yeung et al. reference because then the electropherograms can be accurately compared, with distortions due to a difference in sample volumes, for example (col. 9, ll. 43-49 in the Liu et al. reference).

9. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider et al. (US 6,537,432) in view of Chen (US 5,139,630).

The Schneider et al. reference teaches a method for separating components of a sample (abstract), comprising

obtaining a first separation of the sample components, wherein the sample components are at least partially resolved on the basis of an isoelectric point of each component (col. 22, ll. 8-27);

using an electric field to obtain a second separation of the sample components within a plurality of substantially isolated channels (col. 22, ll. 8-27); and

obtaining an intensity-time data record from each of the isolated channels, the intensity-time data records containing peaks (implied by col. 22, ll. 25-31, which teaches detecting separated species).

The Schneider et al. reference does not specifically mention normalizing a migration time of a first peak with respect to a migration time of at least a second peak to correct for migration time differences between the isolated channels.

The Chen reference teaches normalizing a migration time of a first peak with respect to a migration time of at least a second peak to correct for migration time differences of the same compounds between different runs (col. 2, ln. 41 – col. 3, ln.22 and col. 3, ln. 24 – col. 4, ln. 24).

It would have been obvious to one with ordinary skill in the art at the time the invention was made to normalize a migration time of a first peak with respect to a migration time of at least a second peak as taught by the Chen reference in the invention taught by the Schneider et

al. reference because this will allow rapid and reliable identification of sample peaks without resort to visual identification guesswork (col. 3, ll. 13-22 in the Chen reference).

Allowable Subject Matter

10. Claim 5 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. Claims 10 and 14-16 would be allowable if rewritten to overcome the rejection under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

12. The following is a statement of reasons for the indication of allowable subject matter:

a) Claim 5 requires "determining an average migration time for a plurality of reference sample peaks and determining the product of the ratio and the average migration time." The Yeung et al. reference as modified by the Chen reference does not disclose determining an

average migration time. In the Yeung et al. reference as modified the Chen reference each peak migration is corrected by comparison to a migration time of a reference peak;

b) Claim 10 requires "determining an average intensity for a plurality of reference sample peaks and determining the product of the ratio and the average intensity." The Yeung et al. reference as modified by the Liu et al. reference does not disclose determining an average peak intensity. In the Yeung et al. reference as modified the Liu et al. reference each peak intensity is scaled relative to selected reference peak intensity;

c) Claim 14 requires an autosampler to collect fractions of eluants from the first separation component. The Yeung et al. reference as modified by the Chen reference does not disclose such an autosampler. In the Yeung et al. reference as modified by the Chen. reference junction **32**, which connects the first separation component to the second separation component, is only configured to allow for sample injections, heating, buffer flow, waste collection, and for maintaining electrical contact for electrophoresis and electrokinetic injection (col. 13, ll. 1-24 in the Yeung et al. reference); and

d) Claims 15 and 16 depend directly or indirectly from allowable claim 14.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (703) 305-5686. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (703) 308-3322. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

Alex Noguerola
Alex Noguerola
9/11/2003
Primary Examiner
TC 1700